who had recurrent multiple PMs limited to a different ipsilateral lobe after complete surgical resection.

2. Case report

2.1. Patient 1

A 69-year-old man with a history of pulmonary tuberculosis was referred to our hospital because of a nodular shadow in the lower field of the right lung. Computed tomography (CT) of the chest also showed a 2.5-cm diameter nodular shadow containing a cavity in segment 10 of the right lower lobe (Fig. 1A). The patient received a clinical diagnosis of stage IA lung adenocarcinoma and underwent right lower lobectomy with lymph-node dissection. The postoperative pathological examination revealed a 2.6-cm diameter adenocarcinoma of the papillary subtype that had invaded both lymphatic vessels and blood vessels and metastasized to lymph-nodes 3, 7, and 10. The pathological stage was T1N2M0 stage IIIA. The patient received three cycles of postoperative chemotherapy with cisplatin (80 mg/m^2 on day 1) and vindesine (3 mg/m^2 on days 1 and 8). After receiving adjuvant treatment, he was followed-up at the outpatient clinic of our department. A chest CT scan 19 months after the operation showed multiple pulmonary nodules in the remaining ipsilateral lobes (Fig. 1B). All multiple nodules gradually increased in size over several months, and recurrence of lung cancer was, therefore, diagnosed. No metastasis to distant sites was observed during the progression, and a completion pneumonectomy was performed in accordance with the patient's wishes 10 months after the recurrence was detected. A postoperative pathological examination confirmed multiple metastatic adenocarcinomas of a papillary subtype which were similar to the primary lesion (Fig. 2A). The pathological specimen also showed invasion of blood vessels and lymphatic vessels and the presence of a cluster of cancer cells in a small bronchus (Fig. 2B—D). The patient did not receive any further treatment after the second operation and is doing well without recurrence 7 years after the second operation.

2.2. Patient 2

A 55-year-old woman underwent lobectomy for adenocarcinoma of the left upper lobe at another hospital. The pathological stage was T2N0M0 with a papillary subtype. Pathological examination revealed that the tumor had invaded the viscreal pleura (p2) and lymphatic vessels but not blood vessels. Nine months after surgery multiple pulmonary nodules were detected in a different ipsilateral lobe, the remnant left lower lobe (Fig. 3A). The patient was thereafter referred to our hospital, where recurrent adenocarcinoma was diagnosed on the basis of findings of CT-guided fine-needle biopsy. She thus received three regimens

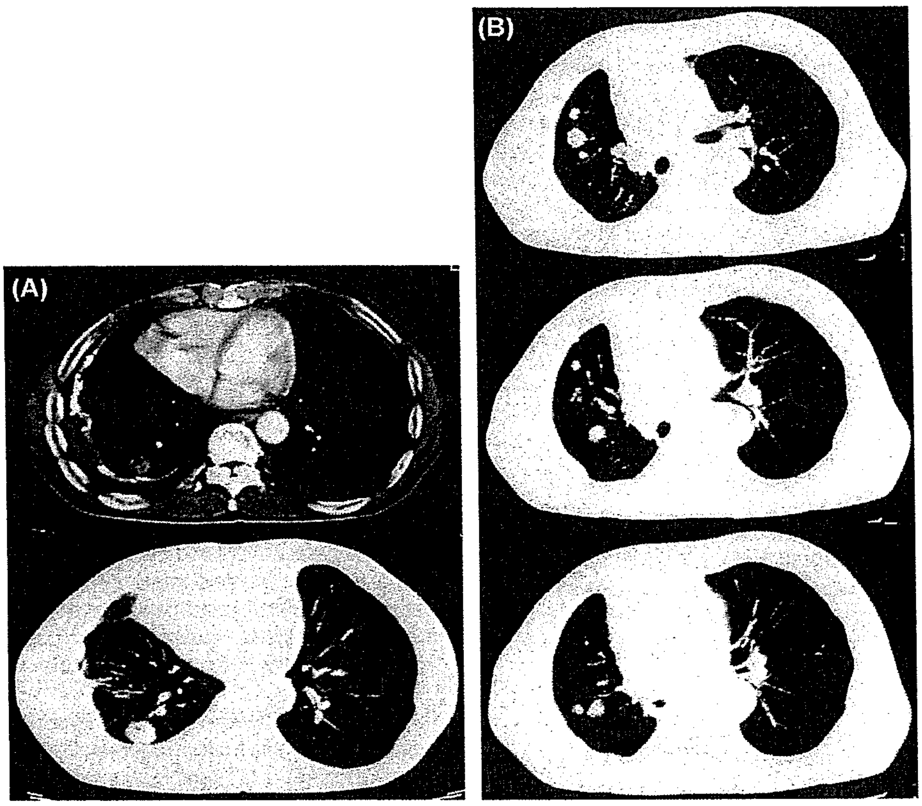

Fig. 1 An axial CT image of patient 1 at the first operation shows a small nodule with a cavity in the right lower lobe (A). Axial CT images of patient 1 at the second operation show multiple small nodules in different ipsilateral lobes but no nodules in the contralateral lung (B).

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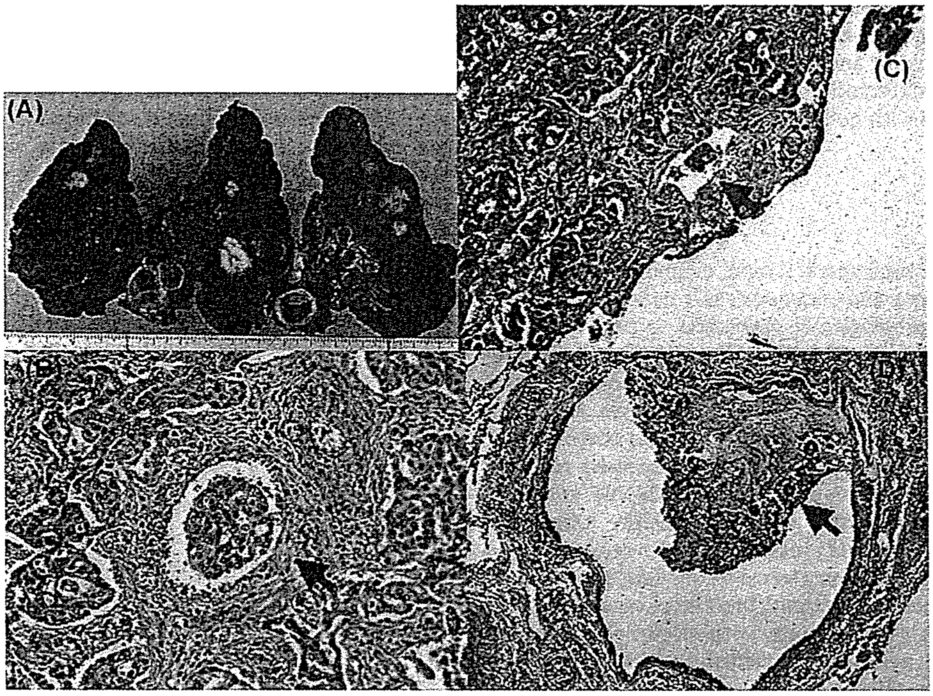

Fig. 2 A gross view of the resected remnant lung after completion pneumonectomy shows multiple metastases (A). Pathological examination of the resected lung shows blood-vessel invasion (B), lymphatic vessel invasion (C), and a cluster of cancer cells in a small bronchus (D).

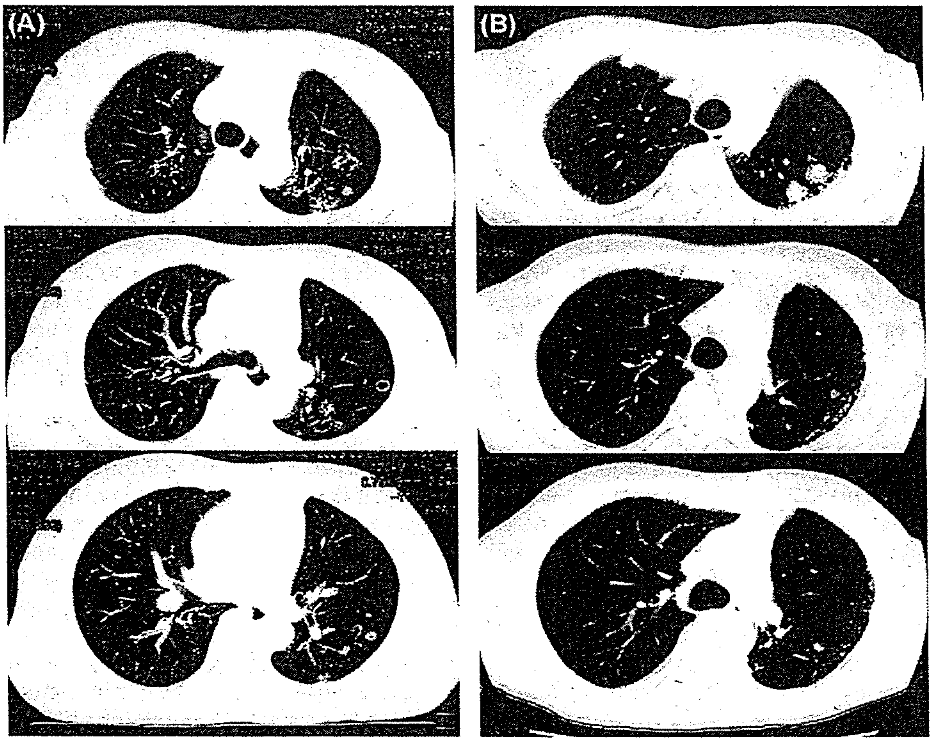

Fig. 3 Axial CT images obtained at the time of recurrence show multiple small nodules and cavities (patient 2, A) and multiple small nodules (patient 3, B) in different ipsilateral lobes but no nodules in the contralateral lung.

of platinum-based combination chemotherapy over 2 years and 6 months. During the clinical course, the PMs demonstrated minor shrinkage and progression three times, but no new lesions were detected at other sites. The patient was thereafter treated with gefitinib and has since had a stable disease course.

2.3. Patient 3

A 55-year-old man received a clinical diagnosis of stage IIB lung adenocarcinoma and underwent left upper lobectomy. The tumor was pathologically diagnosed to be adenocarcinoma of a mixed bronchioloalveolar and acinar subtype; the tumor measured 8.0 cm in greatest diameter, but no vessel invasion, pleural invasion, or lymph-node metastasis was observed. Therefore, the postoperative pathological stage was T2N0M0 stage IB. The patient received postoperative chemotherapy with tegafur-uracil (250 mg/m^2/day) for 6 months. A CT scan 6 months after the operation showed multiple pulmonary nodules in the remnant left lower lobe (Fig. 3B), and recurrence of the lung adenocarcinoma was diagnosed. The patient, therefore, received three cycles of systemic chemotherapy with cisplatin (40 mg/m^2 on days 1 and 8), gemcitabine (800 mg/m^2 on days 1 and 8), and vinorelbine (20 mg/m^2 on days 1 and 8). An objective response was observed, and the patient chose surgical treatment with a completion pneumonectomy after undergoing systemic chemotherapy. A postoperative pathological examination confirmed multiple metastatic adenocarcinomas of an acinar subtype which were similar to the resected primary lesion. The patient has not received any further treatment after the second operation and is alive without recurrence 18 months after the PMs were detected and 1 year after the second operation.

3. Discussion

The prognosis of patients with stage IV NSCLC remains poor despite recent advances in chemotherapy; most large phase III trials have shown a median survival time of 8—12 months [6]. In general, PM is considered to be a type of distant metastasis and is classified as stage IV disease in NSCLC. However, when the PM is totally resected and no other metastases are detected at surgery, patients with PM occasionally survive longer than do patients with metastases to other sites. In the 1997 version of the International Union Against Cancer TNM staging system of NSCLC, PM in the same lobe of the primary lesion is classified as T4 disease. In contrast, PM extending to different ipsilateral lobes or to the contralateral lung has been considered to be M1 disease [1]. This classification is supported by some recently published papers [2,3], but not by others [4,5]. Most patients in these studies underwent surgery and were found to have PM during postoperative pathological examinations. Postoperative recurrence usually takes the form of multiple PMs to both lungs; however, to our knowledge, the present paper is the first to describe in detail cases of multiple PMs to a different ipsilateral lobe as a single recurrent site.

We diagnosed the multiple pulmonary nodules of our three patients as recurrences of the resected cancer, rather than as multiple primary lung cancers, on the basis of the following three points. First, all patients had no pulmonary nodules other than the primary tumor at the first operation, after which multiple nodules, more than five lesions, rapidly developed within 6 months to 1 year. We believe that multiple primary adenocarcinomas, namely more than 5 lesions, are unlikely to occur simultaneously in such a short time. Second, pathological examinations of the recurrent lesions showed adenocarcinoma of same histological subtypes as the primary lesions in patients 1 and 3. Third, no independent atypical adenomatous hyperplasia or bronchioloalveolar carcinoma, accompanying the resected lung, was found in the three cases.

The route through which these one-sided metastases occur remains unclear. It seems unlikely that multiple clusters of cancer cells would metastasize to a single lobe of the ipsilateral lung by chance, after traveling through the systemic circulation. Moreover, our patient 1 has had no recurrence for 7 years since the second operation and is assumed to be cancer-free. Malignant disease that has metastasized to multiple distant sites is rarely cured, although cures of patients with either a single metastasis or a small numbers of metastases are sometimes reported. Therefore, such multiple PMs might represent local recurrence thorough a local route within the ipsilateral thorax. Our other two patients have been free of recurrence for 2.5 years and 1.5 years after the recurrent PMs were detected, 9 and 6 months, respectively, after the first surgeries. Both these patients require further follow-up; however, the PM in these patients might represent localized recurrence, for the reasons mentioned above. Okada and colleagues have investigated 89 patients with ipsilateral and synchronous PMs among 889 patients who underwent surgery; they reported no significant difference in the 5-year survival rate between patients with stage IIIB cancer and those with stage IV cancer with PM (31.4% versus 21.7%, $p = 0.31$). In contrast, the 5-year survival rate was significantly worse in patients with stage IV cancer without PM (10.8%, $p = 0.02$) than in patients with stage IV cancer with PM. They concluded that NSCLC with ipsilateral PM represents locally advanced disease rather than systemic disease [4].

According to this point of view, three possible local routes can be proposed: (1) a route through blood-vessel invasion: direct invasion of a central pulmonary artery or a bronchial artery followed by metastasis to the peripheral lung of the ipsilateral side; (2) a route through lymphatic vessel invasion, metastasis to a hilar lymph-node central to the primary site followed by spread to the peripheral site of a different ipsilateral lobe; (3) a route through transbronchial dissemination, a cluster of cancer cells in the sputum spreads to another ipsilateral bronchus. Fujisawa et al. have demonstrated that both blood-vessel invasion and lymphatic-vessel invasion are important factors for evaluating the route of tumor spread in the ipsilateral lung [7]. They have also reported that cases involving PM to sites central to the primary lesion or to different segments have a significantly lower frequency of blood-vessel invasion, thus suggesting the importance of lymphatic-vessel spread as a possible route of PM at the former sites. If the PM to the ipsilateral lung spreads through lymphatic vessels, then this type of tumor spread may represent localized metastasis rather than distant metastasis. In our patient 1, pathological examinations of the recurrent multiple PMs to different ipsilateral lobes revealed invasion of both blood vessels and lymphatic vessels and clusters of cancer cells in the small bronchus. Therefore, the route of recurrence remains unclear.

In conclusion, the M1 subgroup with multiple intrapulmonary metastases of the primary lesion to a different lobe seems to be a heterogeneous category. Some patients with recurrent multiple PMs to a different ipsilateral lobe have a good prognosis after aggressive treatment, including surgery. The PM in such patients might occur through a local route within the ipsilateral thorax.

Conflicts of interest

None declared.

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Radical sublobar resection for small-sized non–small cell lung cancer: A multicenter study

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Objective: At present, even when early-stage, small-sized non–small cell lung cancers are being increasingly detected, lesser resection has not become the treatment of choice. We sought to compare sublobar resection (segmentectomy or wedge resection) with lobar resection to test which one is the appropriate procedure for such lesions.

Methods: From 1992 to 2001, a nonrandomized study was performed in 3 institutes for patients with a peripheral cT1N0M0 non–small cell lung cancer of 2 cm or less who were able to tolerate a lobectomy. The results of the sublobar resection group enrolled preoperatively (n = 305) were compared with those of the lobar resection group (n = 262).

Results: Except for distribution of tumor location, there were no significant differences in any variable, patient characteristics, curability, pathologic stage, morbidity, or recurrence rate. Median follow-up was more than 5 years. Disease-free and overall survivals were similar in both groups with 5-year survivals of 85.9% and 89.6% for the sublobar resection group and 83.4% and 89.1% for the lobar resection group, respectively. Multivariate analysis confirmed that the recurrence rate and prognosis associated with sublobar resection were not inferior to those obtained with lobar resection. Postoperative lung function was significantly better in patients who underwent sublobar resection.

Conclusions: Sublobar resection should be considered as an alternative for stage IA non–small cell lung cancers 2 cm or less, even in low-risk patients. These results could lay the foundation for starting randomized controlled trials anew, which would bring great changes of lung cancer surgery in this era of early detection of lung cancer.

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In the one and only randomized study to compare lobectomy and sublobar resection for stage IA non–small cell lung cancer (NSCLC) published in 1995, the Lung Cancer Study Group (LCSG) demonstrated a 3-fold increase in the local recurrence rate among patients who underwent sublobar resection,[1] and powerfully supported the indisputable dogma that lobectomy is the standard of care for stage I NSCLC. However, the most broadly referenced report included potentially misleading statements and analyses insufficient to advocate the superiority of lobectomy over sublobar resection as some investigators then and later demonstrated.[2-4]

With the dramatic upsurge in early detection of ever smaller NSCLCs through the development of radiographic tools such as high-resolution computed tomography (CT) and the widespread practice of low-dose helical CT for screening,[5] which is rapidly changing clinical practice, many surgeons have inevitably become concerned over the unified treatment of these small peripheral lesions with whole lobectomy. Generally, patients with a larger tumor have a poorer prognosis and a

Abbreviations and Acronyms

CT	= computed tomography
FEV_1	= forced expiratory volume in 1 second
FVC	= forced vital capacity
LCSG	= Lung Cancer Study Group
NSCLC	= non–small cell lung cancer

higher frequency of hematogenous and lymphatic metastases, whereas smaller tumors such as bronchioloalveolar carcinoma usually have a more indolent biologic behavior. Is it uniformly required to extirpate the entire lobe for such tiny peripheral lesions when sufficient margins of resection can be achieved with sublobar resection? Removing a relatively large volume of healthy lung tissue may result in a higher frequency of operative morbidity and poorer quality of postoperative life, reducing the chance for further resections because these patients survive long enough to be at risk for a second or even a third NSCLC. The incidence of second primary lung cancers may be approximately 3% per year[6,7]; thus patients who survive 5 or more years after their first resection would face a significant cumulative danger of second cancers. The larger the amount of the initial resection, the more restricted the surgical options for next resections.

Recently, several reports demonstrated that sublobar resection was not inferior to lobectomy regarding the prognosis of patients with small-sized NSCLC,[8-13] but the number of cases evaluated in those studies was relatively small. The present study, in which we compared the outcome of sublobar resection with that of lobectomy in low-risk noncompromised patients with a T1N0 NSCLC 2 cm or less in size, is the largest series published so far on radical sublobar resection and followed for long-term outcome. The rigid consensus on lobectomy for stage I cancers has never permitted us to carry out a randomized study. In such a situation in which it has been difficult even to plan a randomized trial because of ethical reasons, a well-designed observational trial may function as an effective reference for a future randomized trial. This was a nonrandomized study in which the decision on whether to be assigned to the sublobar resection group or the lobar resection group was taken by the patients themselves. Because the 2 groups were well matched for known prognostic variables, a comparison between the 2 groups was considered scientifically valid.

Methods

Patients

In 3 institutes during a 10-year period, from January 1992 to December 2001, patients were enrolled for entry into this study when they had a clinical T1N0M0 peripheral tumor of 2 cm or less in every dimension located in the outer one third of the lung on CT confirmed to be an NSCLC. Patients included in the study were able to tolerate a lobectomy as evaluated by cardiopulmonary functional tests, had no history of previously treated cancer, and provided his/her informed written consent based on the approved protocol of each institute's review board before registration and surgery. Patients with a tumor located in the right middle lobe were excluded. Radionuclide bone scan and CT examination of the brain, chest, and upper abdomen were routinely required to detect possible metastases. At the time of registration, every patient was assigned to undergo lobectomy or sublobar resection in compliance with his/her decision. In other words, patients were allocated to the sublobar resection group if the patient consented to the sublobar resection, and to the lobectomy group if the patient did not consent to sublobar resection. Patients were invariably scheduled to undergo lobectomy or sublobar resection before the thoracotomy. During the operation, the tumor status was confirmed by the surgeon to be T1N0 on the basis of frozen-section analysis of sampled segmental, lobar, hilar, and mediastinal lymph nodes from the drainage area of the tumor and pleural lavage cytology. In patients assigned to the sublobar resection group, the surgeon cautiously evaluated the appropriateness of a sublobar resection for curative treatment and whether the deliberate procedure would be a segmentectomy or an adequate large wedge resection. Basically, the wedge resection could be used as a sublobar resection for a tumor of 1.5 cm or smaller in diameter and a tumor observed as pure ground-glass opacity by CT, when considered appropriate. Resected specimens were examined histopathologically, and histologic typing was done according to the World Health Organization classification.[14] Surgical–pathologic staging was performed according to the New International Staging System for Lung Cancer.[15]

Surgical Procedure of Segmentectomy

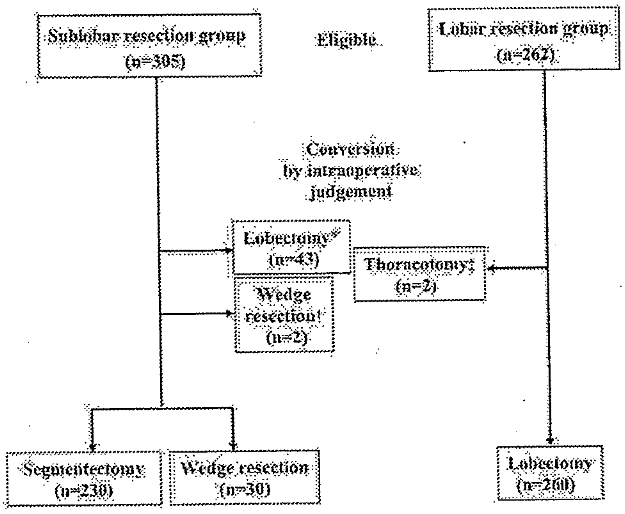
At the hilum, isolation, division, and suture of the suitable segmental bronchus, artery, and vein were required. Intraoperatively, lymph nodes around the hilum and those obtained by mediastinal dissection or sampling were pathologically examined. Surgeons were allowed some latitude regarding the technique to detect and divide the intersegmental plane, including the use of electrocautery, neodymium-yttrium-aluminum garnet laser, or segmental stapling. Because a margin of at least 2 cm of healthy lung tissue was required, the resection line could be placed on the segment adjacent to the affected one or portions of a few adjacent segments or subsegments could be extirpated. After the resection, the surgeon was obliged to corroborate that the tumor and required lymph nodes had been completely removed and proven to be negative for involvement by frozen-section examination. It was specified that when the surgical margin was found to be imperfect or any lymph node was found to be diseased, lobectomy had to be performed instead.

Postoperatively, all complications including minor ones were recorded. Every patient was evaluated at 3-month intervals for the first 2 years, at 6-month intervals for the subsequent 3 years, and yearly thereafter. Follow-up assessment included physical examination, hematologic and biochemical analysis including tumor markers, and chest roentgenograms. Local recurrence was defined as recurrence at the primary site or in lymphatic drainage areas, either hilar or mediastinal within the operated thoracic cavity.

TABLE 1. Base-line characteristics of the patients

Characteristic	Sublobar resection group (n = 305)	Lobar resection group (n = 262)	P value
Gender			0.8655
Male	167 (54.8%)	146 (55.7%)	
Female	138 (45.2%)	116 (44.3%)	
Age (years)	35-82 mean: 63.2	38-84 mean: 64.0	0.3312
Histology			0.4772
AD	276 (90.5%)	229 (87.4%)	
SQ	27 (8.9%)	30 (11.5%)	
AS	2 (0.7%)	3 (1.1%)	
Size			0.0564
Range	5-20 mm	8-20 mm	
Mean	15.7 mm	16.2 mm	
0-10 mm	36	21	
11-20 mm	269	241	
Location			0.0191
Right upper lobe	101 (33.1%)	112 (42.7%)	
Right lower lobe	54 (17.7%)	54 (20.6%)	
Left upper lobe	106 (34.8%)	63 (24.0%)	
Left lower lobe	44 (14.4%)	33 (12.6%)	

AD, Adenocarcinoma; *SQ*, Squamous cell carcinoma; *AS*, Adenosquamous carcinoma. Fisher's exact test was used to compare categoric variables, and student's *t* test was used for continuous data.



*Reasons for conversion to lobectomy: surgical N1 disease, n=11; surgical N2 disease, n=9; insufficient margin, n=23.
†‡ Reason for conversion to wedge resection or toracotomy only: pleural dissemination (n=4).

Figure 1. Treatment flow chart.

Distant metastasis was defined as intrapulmonary metastasis or metastasis to other organs. Pulmonary function tests comprising forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), were administered preoperatively and at 2 months after surgery.

Statistical Methods

Fisher's exact test was used for intergroup comparison of categoric variables, and the Student *t* test was used for continuous data. Survivals were estimated by the Kaplan-Meier method,[16] and differences in survival were determined by log-rank analysis. Multivariate analysis with preoperative prognostic stratification variables was done using Cox proportional hazards regression model.[17] Zero time was the date of pulmonary resection, and the terminal event was death attributable to cancer, non-cancer, or unknown causes for overall survival analysis. Operative mortality defined as a 30-day postoperative death was included in the survival analyses. Disease-free survival was the interval from the date of resection to proven detection of recurrence or metastases. Recurrent disease was defined as the discovery of any new lesion considered to be recurrence of the original lung cancer. All patients were followed until death or study termination, unless lost to follow-up. Analyses of potential survival differences within subgroups and of potential prognostic factors were reported with 2-sided *P* values.

Results

Of the 567 patients preoperatively enrolled, 305 (53.8%) were assigned to the sublobar resection group and 262 (46.2%) were assigned to the lobar resection group. There were no significant differences in gender, age, or histologic type between the 2 groups (Table 1). The mean size of the tumor was a little smaller in the sublobar resection group, although the observed difference was of borderline statistical significance ($P = .0564$). However, location of the tumor was not well balanced ($P = .0191$). Patients with a tumor in the right upper lobe tended to be allocated to the lobar resection group, whereas those with a tumor in the left upper lobe tended to be assigned to the sublobar resection group.

During the operation, the planned procedures were changed for various reasons (Figure 1). Forty-three of the 305 patients in the sublobar resection group underwent lobectomy. Among them, sufficient surgical margins were not obtained in 23 patients, N1 disease was diagnosed in 11 patients, and nodes were judged to be N2 positive intraoperatively in 9 patients. In addition, noncurative wedge resection was carried out in 2 patients because pleural dissemination was found at the time of thoracotomy. Thus, 260 patients in the sublobar resection group underwent operation as planned, 230 patients underwent segmentectomy, and 30 patients underwent curative wedge resection. In contrast, thoracotomy without removal of the tumor was performed in 2 of the 262 patients enrolled in the lobar resection group because of pleural dissemination.

The median follow-up of living patients in the sublobar and lobar resection groups was 72 months (range, 29-155

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TABLE 2. Postoperative findings of the patients

Characteristic	Sublobar resection group (n = 305)	Lobar resection group (n = 262)	P value
Curability			0.2577
Complete resection	303 (99.3%)	257 (98.1%)	
Incomplete resection	2 (0.7%)	5 (1.9%)	
Pathological stage			0.7819
IA	266 (87.2%)	217 (82.8%)	
IB	7 (2.3%)	10 (3.8%)	
IIA	10 (3.3%)	12 (4.6%)	
IIB	2 (0.7%)	2 (0.8%)	
IIIA	14 (4.6%)	15 (5.7%)	
IIIB	6 (2.0%)	6 (2.3%)	
Postoperative complications	20 (6.6%)	19 (7.3%)	0.7429
Recurrence	43 (14.1%)	45 (17.2%)	0.3524
Distant metastasis	28 (9.2%)	27 (10.3%)	
Local recurrence	15 (4.9%)	18 (6.9%)	

Fisher's exact test was used to compare categoric variables.

months) and 71 months (range, 22-158 months), respectively. There were no significant differences between the 2 groups in curability, pathologic stage, incidence of postoperative complication, and recurrence (Table 2). It is noteworthy that the rate of local recurrence did not differ significantly between the 2 groups. Particularly, the recurrence in the remaining part of the affected lobe that we had intentionally preserved with sublobar resection was our prime concern. Among the 260 patients who underwent curative sublobar resection, recurrence was detected in the residual part in 3 patients (1.2%). One patient who underwent segmentectomy of the left upper division for squamous cell cancer showed recurrence in the surgical margin 5 months after surgery and is alive at 87 months after left completion pneumonectomy. Another patient presented a pulmonary metastasis just in the remaining portion at 49 months after right S2 segmentectomy for adenocarcinoma and is alive at 16 months after completion lobectomy. The third patient with right S3 segmentectomy for papillary adenocarcinoma had occurrence of bronchioloalveolar carcinoma at 40 months postoperatively and is surviving at 38 months after completion lobectomy. All 3 patients are free of disease at the time of this report. There was only 1 operative death in the sublobar resection group. The patient died of acute myocardial infarction 29 days after surgery, although he had been discharged from the hospital after a quick uneventful recovery.

Survival

Figure 2 shows the disease-free and overall survivals of the sublobar resection group and lobar resection group, demonstrating no significant differences between them (P = .2778 and P = .106, respectively). Moreover, multivariate analysis using potential preoperative prognostic determinants revealed that irrespective of gender, age, histologic type, tumor size, and tumor location, the disease-free interval and prognosis in the 2 groups were similar (Table 3; hazard ratio, 1.241, P = .3024 and hazard ratio, 1.363, P = .1537, respectively). Next, we examined the surgical outcome in patients who underwent curative resection for pT1N0M0 disease (Figure 3). Not surprisingly, the survival after curative wedge resection was good because the procedure had been indicated for smaller tumors with possibly indolent biologic behavior. Both the disease-free and overall survivals were comparable in patients in p-stage IA whether treated with segmentectomy or lobectomy.

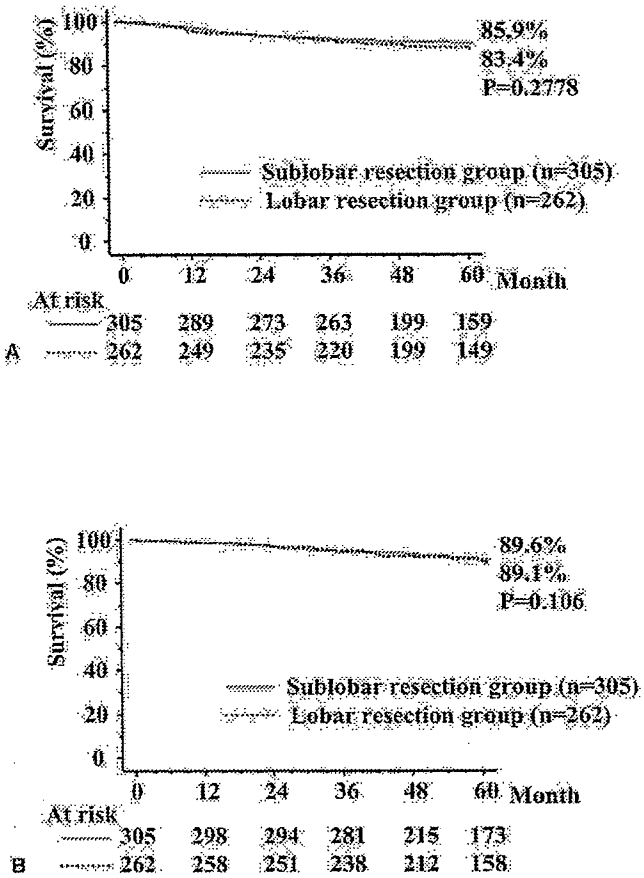

Figure 2. Disease-free survival (A) and overall survival (B). Curves correspond to patients who were initially enrolled for this study (sublobar resection group, *solid line*; lobar resection group, *short-dash line*).

Pulmonary Function

Because lung function tests were not mandatory for this study, information regarding the testing completed pre-

TABLE 3. Proportional hazard model

Variables	Disease-free survival: Relative risk	Disease-free survival: *P* value	Overall survival: Relative risk	Overall survival: *P* value
Gender				
Male (vs Female)	1.761	0.0105	1.568	0.0531
Age				
Older	1.012	0.2761	1.030	0.0168
Histology				
Non-AD (vs AD)	0.526	0.0909	1.149	0.6360
Size				
Larger	1.098	0.0058	1.022	0.4994
Side				
Left (vs Right)	1.307	0.2004	1.200	0.3976
Lobe				
Upper (vs Lower)	1.483	0.1041	1.576	0.0667
Enrolled group				
Lobar (vs Sublobar)	1.241	0.3024	1.363	0.1537

AD, Adenocarcinoma. Continuous data for age and size, and categories for gender, histology, side, lobe, and enrolled group.

operatively and postoperatively was available on 354 patients (62.4%). We analyzed the data according to the procedure actually executed. Preoperative functional values were similar among the groups who underwent wedge resection (n = 18), segmentectomy (n = 168), and lobectomy (n = 168), confirming that patients in the sublobar resection group could have functionally tolerated a lobectomy (Table 4). In regard to both FVC and FEV_1, the extent of resection seemed to correlate with the reduction of lung function. Next, we directly compared functional changes between the 3 groups. Figure 4 clearly demonstrates that the greater the resected amount of tissue, the more reduced the postoperative pulmonary function. Statistically significant differences in the ratio of postoperative to preoperative FVC and FEV_1 were observed among the 3 groups, although a marginal difference in FVC was seen between the segmentectomy group and the wedge resection group.

Discussion

It is of utmost importance to adequately resolve a controversial issue concerning the choice of resection for peripheral small early-stage NSCLCs, because the detection rate of these lesions potentially amenable to effective treatment with lesser resection has dramatically increased in recent years. In 1995, the LCSG reported 1 randomized study concluding that lobectomy was the standard of care for stage IA NSCLCs,[1] which made a great impact on the following advance of lesser resection, although most recent studies comparing lesser resection with lobectomy for stage IA NSCLC demonstrated equivalent survival.[8-13] Patel and

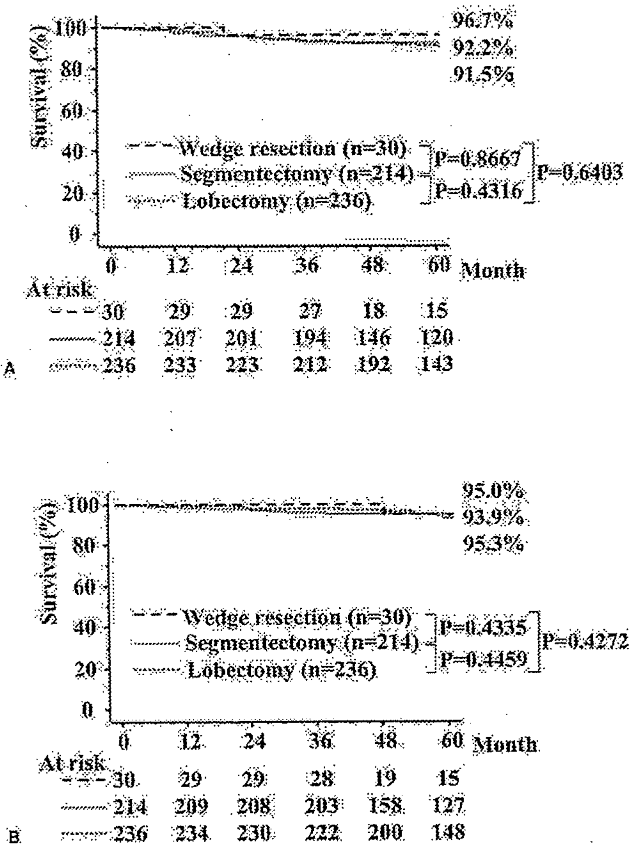

Figure 3. Disease-free survival (A) and overall survival (B). Curves correspond to patients who underwent curative resection for pT1N0M0 tumor (wedge resection, *long-dash line*; segmentectomy, *solid line*; lobectomy, *short-dash line*).

colleagues[4] raised several doubts about the analysis and interpretation of the results of the LCSG study. Their review of the LCSG trial outcome suggested that patients with lesser resections may be at a higher risk of developing local recurrence, lower rate of perioperative lung morbidity, similar cancer-related mortality rate, and better preservation of lung function compared with lobectomy for stage IA NSCLC. Table 5 shows a review of the literature regarding the survivals after resection of stage IA (T1N0M0) NSCLC.[1,8,9,12,18,19]

The LCSG study showed a high incidence of local recurrence after sublobar resection, which we did not find in our series, although the methods of follow-up such as serial CT have been rapidly evolved year after year to identify local recurrence. We are focusing on the high rate of wedge resection in the sublobar resection group (32.8%), although the LCSG study involved stage IA cancers including tumors up to 3 cm in diameter. The predominance of wedge resection might affect the frequency of local recurrence. In our

TABLE 4. Changes of lung function

Procedure	Preoperative values	→	Postoperative values
Wedge resection (n = 18)			
FVC (L)	3.30 ± 0.81	→	3.10 ± 0.69
FEV1.0 (L)	2.29 ± 0.59	→	2.21 ± 0.84
FEV1.0/FVC (%)	70.2 ± 12.1	→	71.9 ± 11.5
Segmentectomy (n = 168)			
FVC (L)	3.16 ± 0.84	→	2.83 ± 0.80
FEV1.0 (L)	2.32 ± 0.64	→	2.10 ± 0.62
FEV1.0/FVC (%)	73.7 ± 9.2	→	74.8 ± 10.0
Lobectomy (n = 168)			
FVC (L)	3.19 ± 0.80	→	2.68 ± 0.77
FEV1.0 (L)	2.32 ± 0.58	→	1.93 ± 0.58
FEV1.0/FVC (%)	73.2 ± 8.3	→	72.5 ± 10.2

FVC, forced volume capacity; *FEV1.0*, forced expiratory volume in 1 second.

series, which included tumors up to 2 cm, the ratio of wedge resection was 9.8%. The frequency of local recurrence after sublobar resection could have been lower if the indication had been limited to tumors of 2 cm or smaller. In addition, the reasons for the differences in the occurrence of local recurrence may be associated with our preference to favor extended segmentectomy, which can improve the treated margin.[8,9,12,13] The intraoperative lavage cytology of surgical margins may be useful to check whether resection was complete.[20] On the other hand, frequent application of wedge resection can result in less-extensive intraoperative nodal surveillance, leading to a potential understaging of patients, in contrast with segmentectomy, which allows the assessment of nodal status. We are convinced that nodal assessment is obligatory for tumors larger than 2 cm.[21] We, under strict policy, especially when planning a sublobar resection, must resist the great temptation to perform an easier operation such as wedge resection. Many proficient surgeons have emphasized that segmentectomy must be essential and should not be forgotten by current-generation thoracic surgeons.[22-26]

The LCSG also reported that respiratory failure developed in 6 patients requiring postoperative ventilation for more than 24 hours in the lobectomy group, whereas no patient in the sublobar resection group required ventilatory assistance.[1] Longer ago, the LCSG found that the operative mortality was 6.2% after pneumonectomy, 2.9% after lobectomy, and 1.4% after sublobar resections in a universe of 2220 resections for lung cancer.[27] Preserving lung parenchyma can contribute to a lower occurrence of lung dysfunction, complications, and operative deaths, which suggests that perioperative morbidity and mortality rates would be improved with a lesser resection.

An important positive result overlooked in the LCSG trial is the advantage of sublobar resection concerning pulmonary function.[1] The FVC, FEV_1, and maximum voluntary ventilation were all significantly better in patients who underwent sublobar resection at 6 months after surgery. At 12 months the FEV_1 was still significantly better. Recent studies have shown superior lung function after lesser resection,[10-12] and more recently Harada and colleagues[28] demonstrated that the extent of removed lung parenchyma by the segment affected that of postoperative functional loss even at 6 months after segmentectomy or lobectomy for lung cancer. Our series revealed that sublobar resection provided better preservation of both FVC and FEV_1 compared with lobar resection at 2 months after surgery. These findings support that sublobar resection obviously offers a functional merit and constitute a more compelling reason to consider sublobar resection as identification of small cancers increases.

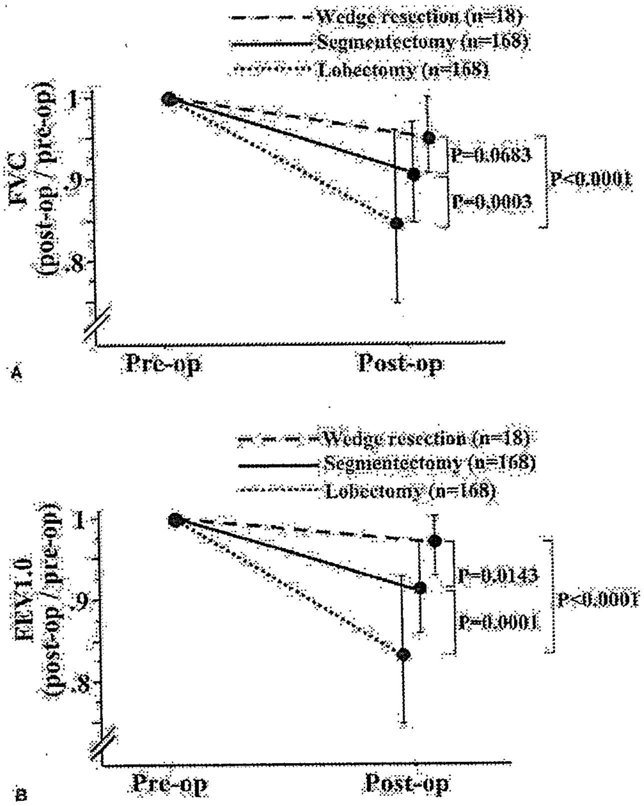

Figure 4. FVC (A) and FEV_1 (B) measured preoperatively and postoperatively (wedge resection, *long-dash line*; segmentectomy, *solid line*; lobectomy, *short-dash line*). Y-axis shows the ratio of the postoperative value to the preoperative one. Values are presented as the mean ± standard error. *FVC*, Forced vital capacity; *FEV_1*, forced expiratory volume in 1 second.

Possibly, not only a diseased margin but also intrapulmonary metastases or involved intralobar nodes might develop in the intentionally preserved lobe after sublobar resection. Under careful follow-up, in our series we identi-

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TABLE 5. Summary of literature in prognosis following sublobar and lobar resection for stage IA(T1N0M0)NSCLC

Author	Sublobar resection Number	Sublobar resection 5-year survival (%)	Lobar resection Number	Lobar resection 5-year survival (%)
Read et al., 1990[18]	113	84	131	74
LCSG 1995[1]	122	44*	125	65*
Kodama et al., 1997[8]	46	93	77	88
Landreneau et al., 1997[19]	102	62	117	70
Okada et al., 2001[12]	68	87	104	87
Koike et al., 2003[9]	74	89	159	90
The present study	305	89.6	262	89.1

NSCLC, non-small cell lung cancer. *statistically significant.

fied 3 patients with local recurrence in the remaining part of the diseased lobe after segmentectomy. At the time of this report all these patients are alive without disease after completion lobectomy (n = 2) or pneumonectomy (n = 1). In our study, as a result of careful selection of patients and strict procedures, sublobar resection offered no survival demerit over lobectomy. Despite the nonrandomized nature of our study, our data force us to suggest that sublobar resection with sufficient margin and nodal assessment should provide appropriate treatment for stage I NSCLC of 2 cm or smaller in lieu of lobectomy in this era of increasing early discovery of small-sized lung cancer. We hereafter might consider the correlation between CT findings and bronchioloalveolar carcinoma component in the selection of patients for radical sublobar resection.[29] At present, the time is ripe for a large randomized trial, which would greatly change the standards of surgical treatment for lung cancer in the near future.

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Selective Mediastinal Lymphadenectomy for Clinico-Surgical Stage I Non–Small Cell Lung Cancer

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Selective Mediastinal Lymphadenectomy for Clinico-Surgical Stage I Non–Small Cell Lung Cancer

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Background. Improved radiologic imaging provides earlier detection of non–small cell lung cancer, but controversy exists regarding the need for complete lymph node dissection. This study was designed to evaluate the possibility of lesser mediastinal dissection for early-stage lung cancer.

Methods. Selective mediastinal dissection is defined as follows: Dissection of the upper mediastinum for upper-lobe tumors is performed but it is not needed for lower-lobe tumors with intact hilar and lower mediastinal nodes. Also, dissection of the lower mediastinum for an upper-lobe tumor is not routinely required when the nodes in the hilum and upper mediastinum are negative. From 1997 through 2002, 377 patients with clinico-surgical stage I non–small cell lung cancer underwent curative-intent surgery with selective dissection (group S). In addition, 358 patients with the same-stage disease who underwent complete lymphadenectomy by the same surgical team served as historic controls (group C).

Results. The characteristics of the two groups were well balanced. There was no significant difference in disease-free survival ($p = 0.376$) or overall survival ($p = 0.060$). Multivariate analysis showed that the dissection mode did not significantly influence either disease-free survival ($p = 0.636$) or overall survival ($p = 0.119$). The postoperative morbidity rates were 17.3% and 10.1% for group C and group S, respectively ($p = 0.005$). One operative death occurred in each group (0.3%). The rates of distant metastasis and local recurrence were similar in the two groups.

Conclusions. Selective mediastinal dissection for clinico-surgical stage I non–small cell lung cancer proved to be as effective as complete dissection, and although large multicenter trials are warranted, it might be considered as an alternative for curative surgery in this era of minimally invasive surgery.

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Up to the present, there has been no consensus among thoracic surgical oncologists regarding the optimal dissection of mediastinal lymph nodes for patients with early-stage non–small cell lung carcinoma (NSCLC). There have been two contrasting opinions concerning its significance. On the one hand, it has been traditionally advocated that lymphadenectomy is important for survival as well as for staging. On the other hand, lymphadenectomy has been considered to be only useful for staging with no influence on the prognosis because cancer is a systemic disease even at its origin. Current surgical practice varies from mere visual inspection of the unopened mediastinum to radical lymphadenectomy. Although for an accurate staging of NSCLC it is necessary to examine the mediastinal lymph nodes, the extent of their removal has been a matter of debate. Whereas lymphadenectomy may contribute to prolong the time to recurrence and survival, the operative time, blood loss, and the frequency of recurrent laryngeal nerve injury, chylothorax, and bronchopleural fistula are increased.

As a result of the development of radiographic tools such as high-resolution computed tomography, the frequency of detection of early-stage lung cancer has been dramatically increasing. If the use of low-dose helical computed tomography to screen patients for the presence of lung cancer becomes a more widespread practice, we will probably encounter an escalating number of very early cancers with indolent biologic behavior in the near future and find ourselves in a tremendous dilemma regarding the extent of nodal dissection as well as of lung tissue removal. Thus, it is important to develop a more reasonable approach for dissecting mediastinal lymph nodes.

In 1997, we reviewed the clinical records of patients with completely resected NSCLC to assess the features and patterns of mediastinal spread of the tumor cells to lymph nodes, and reported the validation and the utility of selective mediastinal lymph node dissection [1]. Then, we initiated a prospective cohort study of this type of dissection in patients with clinical and surgical stage I disease. We thus sought to evaluate selective mediastinal dissection from the viewpoint of postoperative prognosis to open the gate for large trials.

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Patients and Methods

Selective dissection of mediastinal lymph nodes refers to the dissection of the upper mediastinum including aortic regions, performed regardless of the operative appearance when the tumor is located in the upper lobe, but not when it is located in the lower lobe and the hilar and lower mediastinal nodes are negative. Besides, dissection of the lower mediastinum in patients with an upper-lobe tumor is not needed when the nodes in both the hilum and upper mediastinum are intact. During the operation, dissected lymph nodes were aggressively sent to the pathologist for rapid examination of frozen sections.

Patients

Between January 1997 and December 2002, 463 consecutive patients with clinical stage I NSCLC except in the middle lobe, were enrolled into this study. Among them, 377 patients underwent curative-intent surgery with selective dissection of mediastinal lymph nodes. Twenty-six patients were excluded from the study during the operation because of pleural dissemination including positive pleural lavage cytology. The remaining 60 patients, 35 with surgical N1 disease and 25 with surgical N2 disease, underwent complete mediastinal dissection and therefore were excluded. Three hundred fifty-eight patients with clinical and surgical stage I NSCLC were identified as historic controls; these patients had been subjected to curative resection of the tumor and complete dissection of the mediastinum consecutively performed by the same surgical team from January 1985 through December 1996.

Informed consent was obtained from the patients or surrogates. Patients were excluded if they were assigned to chemoradiotherapy, mediastinoscopy was performed to assess nodal status, or they did not meet the definition of stage I disease [2]. Moreover, patients who exhibited residual tumor at the resection margin or had evidence of malignant effusion were excluded. The patients who were excluded from the study were equally allocated to the two groups. Resected specimens were examined histopathologically, and histologic typing was done according to the World Health Organization classification. Local recurrence was defined as any recurrence within the ipsilateral chest cavity, and all other recurrences were classified as distant metastases. Recurrence was evaluated on the basis of clinical findings or images at the follow-up visit, which took place every 3 months. Second primary tumors were excluded from the analysis of recurrence [3]. Operative mortality included all deaths occurring within 30 days after resection.

Grouping of Lymph Node Sites

The sites of N2 lymph nodes were grouped as follows: upper mediastinal (1, highest mediastinal nodes; 2, paratracheal nodes; 3, pretracheal nodes; and 4, tracheobronchial angle nodes), aortic (5, Botallo's nodes; and 6, ascending aortic nodes), and lower mediastinal (7, subcarinal nodes; 8, paraesophageal nodes; and 9, pulmonary ligament nodes) lymph nodes, and N1 comprised hilar (10, main bronchus nodes; 11, interlobar nodes; and 12, lobar nodes) and intrapulmonary (13, segmental nodes; and 14, subsegmental nodes) lymph nodes. Mediastinal metastases were considered as so-called skipping ones if any of the N2 nodes, but no N1 nodes, were involved. Basically, three stations (numbers 10, 11, and 12) of N1 lymph nodes and one station of N2 nodes (number 4 for right upper-lobe tumors, number 5 for left upper-lobe tumors, number 7 for lower-lobe tumors) were examined by frozen section to select the type of dissection. Actually, however, the surgeons decided intraoperatively which stations were to be examined according to the surgical findings of each case.

Statistical Methods

Differences between the two groups were compared using Fisher's exact test for categorical data and Student's t test for continuous variables. Disease-free survival was defined as the time from surgery to first locoregional or distant recurrence. An observation was censored at last follow-up if the patient was alive or if the patient had died from a cause other than the original NSCLC. The overall survival was calculated from the date of surgery to every death. Distribution of disease-free survival and overall survival was estimated with the Kaplan-Meier method and compared using the log-rank test. Cox regression analysis was used to simultaneously determine the relationship between survival and one of the following factors with a potential prognostic value: sex, age, histologic type, size of the tumor, pathologic nodal status, and mode of the dissection.

Results

The median follow-up time was 62 months (range, 28 to 98 months) for the selective dissection group (group S) and 111 months (range, 67 to 207 months) for the complete dissection group (group C). The characteristics of the groups, listed in Table 1, show that the baseline features were well balanced. In group S, 36 patients were diagnosed as having bronchioloalveolar carcinoma, in which the proportion of the bronchioloalveolar carcinoma component was more than 50%. The postoperative complications are shown in Table 2. The morbidity rates were 17.3% and 10.1% for group C and group S, respectively ($p = 0.005$). Dysrhythmia, such as atrial fibrillation, was the most common morbidity after either type of dissection. One operative death secondary to myocardial infarction or cardiogenic shock occurred in group C (0.3%), whereas one operative death owing to septic shock occurred in group S (0.3%).

Regardless of the presence of surgical N0 disease, pathologic nodal factors could be upstaged by final histopathologic examination, which revealed lymph node involvement in 23 patients (6.1%) of group S and in 22 patients (6.1%) of group C. There were 21 patients (5.6%) with N1 disease and 2 patients (0.5%) with N2 disease in group S, whereas 19 patients (5.3%) had N1 disease and 3 patients (0.8%) had N2 disease in group C. No significant differences were found regarding patient character-

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Table 1. Patient Characteristics

Variables	Complete Dissection (n = 358)	Selective Dissection (n = 377)	p Value[b]
Sex			
Male	240 (67.0%)	234 (62.1%)	0.166
Female	118 (33.0%)	143 (37.9%)	
Age (y)	30–85 (mean, 65)	20–83 (mean, 65)	0.822
Histology			
AD	233 (65.1%)	274 (72.7%)[a]	0.118
SQ	108 (30.2%)	82 (21.8%)	
AS	5 (1.4%)	4 (1.1%)	
LA	5 (1.4%)	7 (1.9%)	
Other	7 (2.0%)	10 (2.7%)	
Size (mm)	5–90 (mean, 29.3)	5–75 (mean, 27.7)	0.864
pN status			
pN0	336 (93.9%)	354 (93.9%)	0.719
pN1	19 (5.3%)	21 (5.6%)	
pN2	3 (0.8%)	2 (0.5%)	

[a] Including bronchioloalveolar carcinoma (n = 36). [b] Fisher's exact test or χ^2 test test was used to compare categoric data, and Student's *t* test was used for continuous variables.

AD = adenocarcinoma; AS = adenosquamous carcinoma; LA = large cell carcinoma; SQ = squamous cell carcinoma.

istics between those with metastasis and those who did not have metastasis ($p = 0.719$), demonstrating no discrepancy in the surgical N0 false-negative value between the two groups. Two patients with pN2 disease in group S had adenocarcinoma with a single-station skipping metastasis. One patient had distant metastasis and the other had malignant effusion.

Among the 21 patients with pN1 disease in group S, none had recurrence of mediastinal lymph nodes postoperatively. The recurrence patterns of the two groups are presented in Table 3. Although the difference in follow-up period should be duly considered, recurrence rates regarding distant metastases and local involvement, including mediastinal lymph nodes, were approximately equal in the two groups or a little lower in group S. Statistically, no significant differences were observed.

Table 2. Postoperative Complications

Complication	Complete Dissection (n = 358)	Selective Dissection (n = 377)
Dysrhythmia	19	12
Pneumonia or atelectasis	15	6
Prolonged air leak (>1 week)	14	11
Chylothorax	4	2
ARDS	3	1
Peptic ulcer	3	2
Lung infarction	2	0
Hemothorax	1	3
Myocardial infarction	1	1
Total	62 (17.3%)	38 (10.1%)

ARDS = adult respiratory distress syndrome.

Table 3. Recurrence Pattern of Patients

Dissection	Complete (n = 358)	Selective (n = 377)	p Value
No recurrence	245 (68.4%)	282 (74.8%)	0.067
Recurrence	113 (31.6%)	95 (25.2%)	
Distant metastasis	71 (19.8%)	60 (15.9%)	0.905
Distant metastasis + local recurrence	9 (2.5%)	9 (2.4%)	
Including mediastinal node	6 (1.7%)	6 (1.6%)	
Local recurrence only	33 (9.2%)	26 (6.9%)	
Including mediastinal node	7 (2.0%)	6 (1.6%)	

There was no significant difference in disease-free survival (Fig 1A) or in overall survival (Fig 1B) between the two groups ($p = 0.376$ and $p = 0.060$, respectively). The 5-year disease-free survival for group S and group C was 76.4% and 73.4%, respectively. In addition, the 5-year overall survival for group S and group C was 83.2% and 79.7%, respectively. Because distribution and nature of the dis-

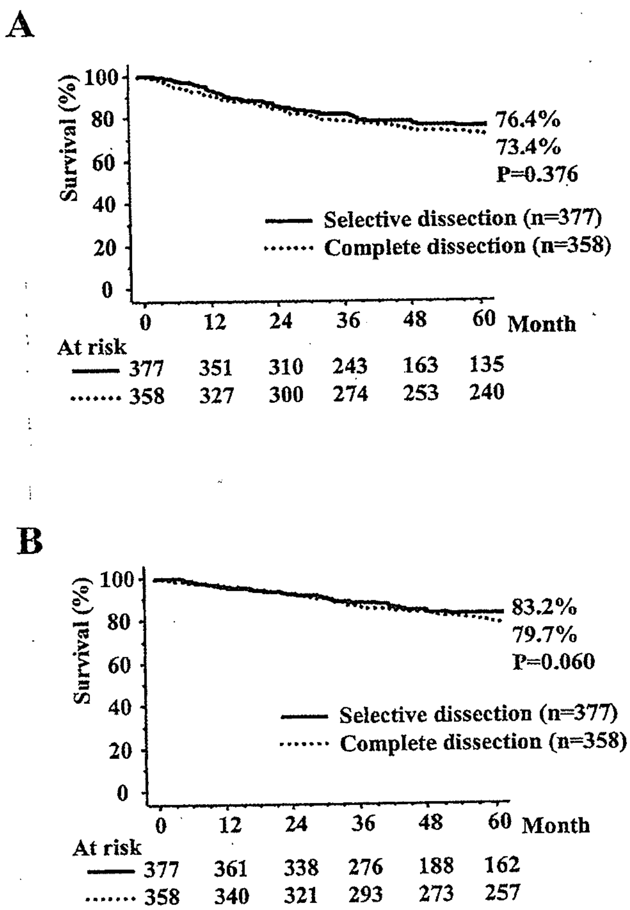

Fig 1. Disease-free (A) and overall (B) survival curves of all patients with clinical and surgical stage I disease, stratified by the type of mediastinal dissection.

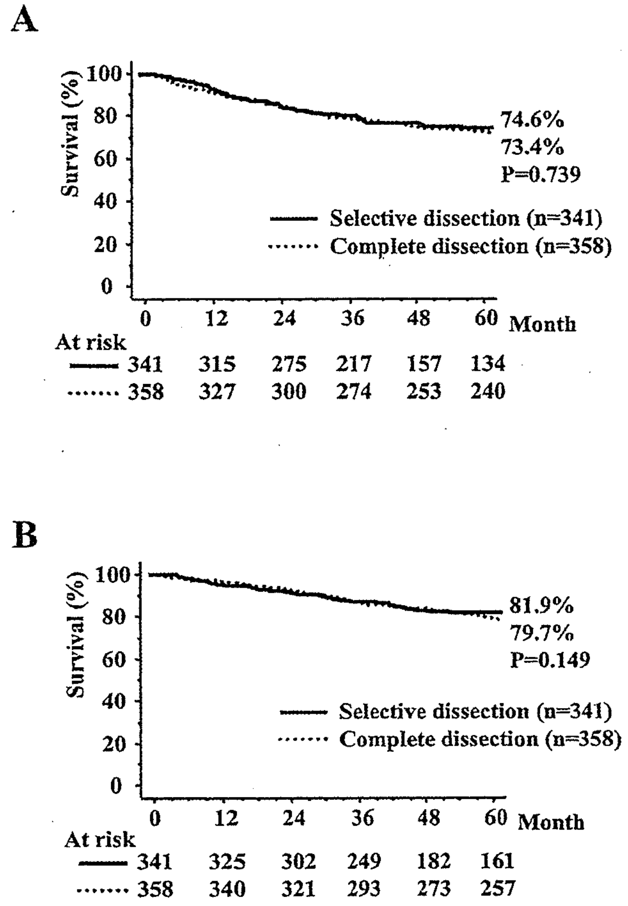

Fig 2. Disease-free (A) and overall (B) survival curves of patients with clinical and surgical stage I disease except those with bronchioloalveolar carcinoma, stratified by the type of mediastinal dissection.

eases have changed after the introduction of high-resolution computed tomography, we additionally analyzed survival except for patients with bronchioloalveolar carcinoma. Even then, no significant differences were found in disease-free survival (Fig 2A) or in overall survival (Fig 2B) between the two groups ($p = 0.739$ and $p = 0.149$, respectively). In the multivariate analysis (Table 4), the type of dissection performed did not significantly affect either the disease-free survival ($p = 0.636$) or the overall survival ($p = 0.119$). Sex, age, tumor size, and pN factor maintained a strong correlation not only with overall prognosis but also with the risk for recurrence.

Comment

The issues to consider when evaluating mediastinal lymph node dissection are the differential benefit to definitive staging and survival, and the possible associated morbidity [4]. Some authors have demonstrated that patients with fewer dissected and pathologically examined lymph nodes showed higher rates of recurrence and death when compared with patients with more nodes assessed [5, 6]. One potential reason is that having more lymph nodes dissected elevates the staging accuracy, thus suitably upstaging the patients who would have otherwise been incorrectly included among stage I patients, which is known as the so-called Will Rogers phenomenon or stage migration [7]. When lymph node sampling is not adequate, the true N stage remains unrecognized, which may produce a false downstaging. Another less likely reason is that extirpation of lymph nodes can be therapeutic. On the other hand, extended dissection may result in higher morbidity.

Nowadays, early-stage lung cancer is being frequently detected, and thus thoracic surgeons wonder whether complete dissection of mediastinal lymph nodes is uniformly required in radical surgery for such lesions. Up to now, there have been two randomized studies published, and neither of them has shown any significant difference of outcome in patients subjected to complete lymphadenectomy when compared with those having undergone sampling [8, 9]. Izbicki and coworkers [8] reported in their randomized trial that complete dissection did not improve survival compared with sampling in patients with no nodal involvement, despite finding that complete dissection had led to better staging of lung cancer. The other randomized study performed by Sugi and colleagues [9] showed that survival of the sampling group was better than that of the dissection group (overall 5-year survival 84% versus 81%); the authors concluded that clinically evaluated lung cancer smaller than 2 cm in diameter did not require radical systematic mediastinal lymph node dissection. They also reported that the morbidity associated with complete dissection was significantly higher than that seen with sampling (23.8% versus 3.4%). Our serious concern regarding these studies is the considerably small number of evaluated cases.

In 1997 we analyzed the patterns of lymph node metastases, including skipping ones, in patients who underwent complete dissection for NSCLC and suggested the possibility of a rational and practical lesser mediastinal dissection, for which sampling and examination of a sufficient number of key lymph nodes were

Table 4. Proportional Hazard Model

		Overall Survival		Disease-Free Survival	
Variables[a]	Worse	Relative Risk	*p* Value	Relative Risk	*p* Value
Sex	Male	1.886	0.0009	1.419	0.033
Age	Older	1.043	0.0001	1.026	0.002
Histology	AD	1.334	0.096	1.983	0.0001
Size	Larger	1.019	0.0003	1.022	0.0001
pN factor	Positive	2.998	0.0001	2.675	0.0001
Dissection		1.315	0.119	1.075	0.636

[a] Continuous variables for age and size, and categories for sex, histology, pN factor, and dissection.

AD = adenocarcinoma.

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extremely important [1, 10]. In case of upper-lobe tumors, we decided lower mediastinal lymphadenectomy was not needed if the hilar and upper mediastinal nodes were found to be tumor-free, and in case of lower-lobe tumors, upper mediastinal lymphadenectomy was not considered necessary when the hilar and subcarinal nodes were found to be tumor-free. Exceptionally, when patients were suspected of having an advanced disease based on their intraoperative findings, such as extent of invasion, a complete lymphadenectomy was routinely performed. Since then, we have introduced such selective mediastinal dissection for clinical and surgical stage I NSCLC. This report describes the first large series representing all patients treated with selective dissection, and compares selective dissection with complete lymphadenectomy. Although this study is limited by factors inherent to all nonrandomized studies that compare data from historic controls operated on by the same team, such as a potential selection bias, it presents two characteristics reinforcing the meaning of its results: the comparison of the two groups of patients proved to be relatively homogeneous regarding the main clinical variables, and the high follow-up rate of treated patients strongly indicates that the patients studied are highly representative of clinical and surgical stage I NSCLC patients surgically treated at our institution. The consecutive nature of the two groups of patients reduces the extent of possible bias.

In our series, the 5-year disease-free survival rate of patients who underwent selective dissection was 76.4% and that of patients who underwent complete dissection was 73.4%. In addition, the 5-year overall survival rate of patients who underwent selective dissection was 83.2% while that of patients who underwent complete dissection was 79.7%. Even when patients diagnosed as having bronchioloalveolar carcinoma, whose number has been increasing with recent advances of radiologic imaging and who would have better prognosis, were excluded from the selective dissection group, there were no significant differences in survival between the two groups. These data demonstrated that selective dissection was not inferior to a complete one regarding prognosis. Although only 1 patient in each group (0.3% each) died during the perioperative period, the postoperative morbidity was significantly higher in the complete dissection group, suggesting that the extent of dissection influenced the frequency of complications. The complications can possibly arise from injury of the bronchial arteries and nerves, recurrent nerves, laryngeal nerves, and the thoracic duct and lymphatic backflow, resulting in ischemic tissue changes, pulmonary edema, and pneumonia as well as respiratory distress syndrome. These results were consistent with those of other studies [9] and suggested that removing healthy lymph nodes should be minimized. At present, we cannot draw definite conclusions about the advantage of selective dissection because of the nonrandomized nature of this study, the lack of a prospective control group, and the fact that more recently treated patients were more likely to have undergone selective dissection. The improved results may be related to improved surgical or postoperative care, improved staging techniques, or other unknown variables that may have led to improved patient outcome in this study. However, we can conclude that although these data may not show the superiority of selective dissection to a complete one, they at least show our approach is not inferior to complete lymphadenectomy.

The question of the extent of mediastinal dissection will become even more important in the future as many surgeons become interested in a minimally invasive surgery such as video-assisted thoracic surgery to treat patients with early-stage NSCLC. We have adopted this type of dissection in case of video-assisted thoracic surgery, during which complete mediastinal dissection is a complex procedure. Therefore, when following the minamally invasive approach, a simpler dissection technique is easier to apply, and recently its need is more keenly felt. However, the current practice of using selective mediastinal lymphadenectomy in curative surgery for clinico-surgical stage I NSCLC should be reevaluated through randomized multicenter trials.

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Selective Mediastinal Lymphadenectomy for Clinico-Surgical Stage I Non–Small Cell Lung Cancer

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A novel video-assisted anatomic segmentectomy technique: Selective segmental inflation via bronchofiberoptic jet followed by cautery cutting

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Objective: Segmentectomy is an anatomic parenchyma-sparing resection that is recently being performed for small-sized lung carcinoma and constitutes a useful procedure in a thoracic surgeon's armamentarium. We have generated a new technique that improves the identification of the intersegmental border and whose clinical utility we evaluate in this study.

Methods: Under bronchofiberscopy, jet ventilation is selectively applied to the burdened bronchus to develop an anatomic plane between the inflated segment to be resected and the deflated area to be preserved. From April 2004 to June 2006, 52 consecutive patients with a clinical T1 N0 M0 peripheral cancer 2 cm or smaller underwent video-assisted segmental resection called hybrid VATS segmentectomy in which electrocautery with no stapler was used to divide the intersegmental plane detected by selective jet ventilation.

Results: Complete resection was achieved in all patients. The median operative time and bleeding during the operation were 155 minutes (range 85-225 minutes) and 60 mL (range 10-210 mL), respectively. The complication rate was 13.5% (7/52), and the most common was concerning air leak. The median duration of postoperative air leak and chest tube drainage was 1 day and 3 days, respectively. There were no in-hospital deaths. There was one case of mediastinal lymph node recurrence and another of metastasis to the brain although there was no case of local recurrence in the surgical margin area.

Conclusions: A novel video-assisted segmentectomy technique for lung cancer is clinically useful. Selective segmental inflation provides an obvious intersegmental plane quickly and easily, allowing a real margin distance in the ventilated segment. Despite the minimally invasive approach, since only the segment to be resected and not the entire lobe is expanded, an appropriate surgical view is possible.

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Pulmonary segmentectomy was first carried out for bronchiectasis in the lingula by Churchill and Belsey[1] in 1939 and had been performed since then in many patients with an infectious disease such as tuberculosis and in selected patients with non–small cell lung carcinoma (NSCLC). However, in the past few decades the frequency of this procedure has considerably decreased because of the advent of antibiotic agents for infections, the improvement of sanitary conditions, the outcome of the randomized study by the Lung Cancer Study Group,[2] demonstrating that sublobar resections including wedge resections resulted in higher rate of local recurrence than did lobectomy in patients with stage IA NSCLC, and the escalating incidence of nonanatomic stapled wedge resection. Consequently, most recent residency programs of thoracic surgery do not include segmentectomy as an obligatory procedure, but several expert thoracic surgeons have advanced that

Abbreviations and Acronyms
NSCLC = non–small cell lung cancer
VATS = video-assisted thoracic surgery

segmentectomy is important as a basic surgical technique and should not be forgotten by current-generation thoracic surgeons.[3-7]

In concordance with the explosive increase of early detected small-sized NSCLCs through the development of radiographic tools and the widespread practice of screening,[8] we have been aggressively performing radical segmentectomy with lymph node assessment not only in high-risk patients but also in good-risk patients with clinical stage IA tumors 2 cm or smaller.[9-12] Lately, we have used a new method to detect the intersegmental plane in segmentectomy that involves selective jet ventilation under bronchofiberscopy. With this method the segment to be removed can be inflated while keeping the segments to be preserved without air. This technique is completely opposite to the conventional method and allows the clear visualization of the intersegmental line between the segment to be resected and the one to be preserved. We can see the real surgical margin in the inflated segment and can get a good surgical field even through video-assisted thoracic surgery (VATS) without having to make an effort to suppress the other segments and lobes with an instrument. In addition, dissection of the anatomic intersegmental plane by electrocautery but not by staple reduces local failure at the margin, one of the unfavorable recurrent patterns, and makes the preserved adjacent segments fully expansive to obtain maximum pulmonary function. In this study, we describe this novel technique through hybrid VATS approach[13] in detail and evaluate its clinical utility.

Materials and Methods

Surgical Procedure of Segmentectomy

Patients are positioned in the lateral decubitus position and the lung is isolated with a double-lumen endotracheal tube. Basically, two skin incisions are built for access with no extracostal muscles or ribs cut. One utility incision for manipulation and another access port for the insertion of a thoracoscope are placed. The surgeon directly observes the hilum of the diseased lobe and individually isolates and severs all the bronchi and vessels, although television monitor guidance is variably used during the procedure when dissecting an area out of direct view, which is called hybrid VATS.[13] More recently, the main access has been opened with a wound retractor made of silicone rubber with no rib spreading. It is crucial to note that the skin incision must be extended without hesitation if the surgeon has difficulty with the surgical view. We favor a backhand grip, holding 30-cm-long scissors (model 101-8098-30; Mayo-Harrington; Stille, Sweden) for sharp dissection, lengthy needle holders, and forceps upside-down. Pleural lavage cytology is examined immediately after the introduction of a thoracoscope to check the subclinical tumor dissemination.[14]

Recognition of the intersegmental plane is accomplished by differential inflation with jet ventilation. After the segmental bronchi are isolated, an anesthesiologist puts a 3.5-mm bronchofiberscope through the double-lumen tube into the orifice of the targeted segmental bronchus. The tip of the bronchofiberscope is recognized at the surgical field because the surgeon can see the light of the tip and lead it to the suitable place of the targeted bronchus, in which high-frequency oscillation is started (40 Hz, working pressure 2 kg/cm^2, HFO Jet Ventilator; Mera, Tokyo, Japan). The diseased segment is inflated while the preserved segments appear collapsed, and a line is formed between the inflated and the deflated lung parenchyma, evidencing the anatomic intersegmental plane.[11] This technique allows the development of a defined plane without air transmission through collateral ventilation, unlike the conventional method. After jet ventilation fills the targeted segment, the distal site of the bronchus is tied to keep the segment inflated, and the proximal site to the tie is transected, leaving a stump of sufficient length so that closure will not occlude other segmental orifices. When more than one segment is to be removed, the surgeon can selectively insert the tip of the fiberscope into each segmental bronchus and inflate one segment after the other. At the central portion around the hilum, the intersegmental plane is approached along the intersegmental vein, and at the peripheral site electrocauterization is used along the inflation-deflation line. With a commercially available fibrin sealant (Bolheal; Chemo-Sero Therapeutic Institute, Kumamoto, Japan), composed of fibrinogen and thrombin and an absorbable polyglycolic acid felt (Neoveil; Japan Medical Planning Co, Kyoto, Japan), the raw surface of the remaining lung prevents air leakage after cutting by cautery. Only when the lung is emphysematous can the surgeon use staplers for dividing the intersegmental plane to keep air leak to a minimum. Since a margin greater than the tumor diameter, that is, at least 2 cm of healthy lung tissue, is required, the resection line can be placed on the segment adjacent to the affected one, or portions of a few adjacent segments or subsegments can be extirpated (Figure 1). Sampling or dissection of segmental, lobar, hilar, and mediastinal lymph nodes followed by frozen-section analysis is mandatory to decide the applicability of segmentectomy. In patients with intentional indication for radical segmentectomy, lobectomy should be performed instead when the surgical margin is judged to be imperfect or any lymph node is found to be diseased. Routinely, the chest is drained with a single chest tube under water seal, which is inserted through the incision initially established for the thoracoscope.

Patients

Between April 2004 and June 2006, 52 consecutive patients with a clinical T1 N0 M0 peripheral NSCLC tumor of 2 cm or less in every dimension on high-resolution computed tomography underwent segmentectomy. Electrocautery with no stapler, not even partially, was used to divide the intersegmental plane. Resected specimens, especially the surgical margin, were examined histopathologically, and histologic typing was done according to the World Health Organization classification.[15] Surgical–pathologic staging was performed according to the New International Staging

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